

### **Amendments to the Claims:**

The following listing of claims replaces all prior listings and versions of claims in this application.

1. (Previously Presented) A polypeptide comprising a single-domain of the variable region of the heavy chain of an antibody molecule, which is soluble and stable and capable of binding a specific antigen of interest, said polypeptide comprising a natural framework scaffold of a mammalian monoclonal antibody without induced mutations or modifications in the original VH/VL interface framework residues, said VH/VL interface comprising a charged residue at position 44, a Leu residue at position 45, and a Trp residue at position 47.
2. (Original) The polypeptide of claim 1 wherein the polypeptide is substantially monomeric.
3. (Previously Presented) The polypeptide of claim 1, wherein the polypeptide is encoded by a polynucleotide isolated from a phage clone selected from a phage-display library comprising recombinant phages expressing a single-domain of the variable region of the heavy chain of an antibody molecule comprising a natural framework scaffold of a mammalian monoclonal antibody without induced mutations or modifications in the original VH/VL interface framework residues, said VH/VL interface comprising a Lys residue at position 44, a Leu residue at position 45, a Trp residue at position 47 and a randomized CDR3.
4. (Previously Presented) The polypeptide of claim 3 wherein the selected phage clone is produced in *E. coli* as insoluble inclusion bodies and the polypeptide isolated therefrom is subsequently refolded in-vitro and purified.
5. (Original) The polypeptide claim 3 wherein the scaffold element representing the VH/VL interface comprises the sequence Lysine-44, Leucine-45, and Tryptophan-47.
6. (Original, Withdrawn) The polypeptide of claim 1 wherein the specific antigen of interest is an immunoglobulin molecule.
7. (Previously Presented, Withdrawn) The polypeptide of claim 3 wherein the CDR3 sequence between residues 95 and 100C comprises the consensus sequence: Gly-X-Ser-Pro-Gln (SEQ ID NO: 6), wherein X represents any amino acid.

8. (Previously Presented, Withdrawn) The polypeptide of claim 3 wherein the CDR3 sequence between residues 95 and 100C is selected from the sequences: Gln-Ser-Gly-Gln-Ser-Pro-Gln-Ser-Ile (SEQ ID NO: 9), and Asn-Gly-Lys-Ser-Pro-Gln-Ala-Ala-Trp (SEQ ID NO: 8).

9. (Previously Presented) The polypeptide of claim 3 wherein the specific antigen of interest is tumor necrosis factor.

10. (Previously Presented) The polypeptide of claim 9 wherein the CDR3 sequence between residues 95 and 100C comprises the sequence: Phe-Pro-Thr-Gly-Asp-Leu-Ala-Glu-Lys (SEQ ID NO: 7).

11. (Previously Presented, Withdrawn) The polypeptide of claim 3 wherein the specific antigen of interest is Streptavidin.

12. (Previously Presented, Withdrawn) The polypeptide of claim 11 wherein the CDR3 sequence between residues 95 and 100C is selected from the sequences: His-Ala-Gln-Arg-Arg-Pro-Trp-Ile-Arg (SEQ ID NO: 15), and Glu-Asp-Pro-His-Pro-Gln-Arg-Gly-Tyr (SEQ ID NO: 16).

13. (Previously Presented, Withdrawn) A peptide capable of binding a specific antigen of interest, said peptide being derived from the randomized sequence of the CDR3 region of a polypeptide comprising a single-domain of the variable region of the heavy chain of an antibody molecule, which is soluble and stable and capable of binding said specific antigen of interest, said polypeptide comprising a natural framework scaffold of a mammalian monoclonal antibody without induced mutations or modifications in the original VH/VL interface framework residues, said VH/VL interface comprising a residue other than Gly at position 44, a Leu residue at position 45, and a Trp residue at position 47.

14. (Previously Presented, Withdrawn) The peptide of claim 13 wherein the polypeptide is encoded by a polynucleotide isolated from a phage clone selected from a phage-display library comprising a plurality of recombinant phage, each of said recombinant phages having an expression vector encoding a single-domain of the variable region of the heavy chain of an antibody molecule comprising a natural framework scaffold of a mammalian monoclonal antibody without induced mutations or modifications in the original VH/VL interface framework residues, said VH/VL interface comprising a Lys residue at position 44, a Leu residue at position 45, and a Trp residue at position 47 and a randomized CDR3.

15. (Original, Withdrawn) The peptide of claim 13 wherein the peptide comprises 4-20 amino acids.
16. (Original, Withdrawn) The peptide of claim 13 wherein the peptide comprises 7-15 amino acids.
17. (Original, Withdrawn) The peptide of claim 13 wherein the specific antigen of interest is an immunoglobulin molecule.
18. (Original, Withdrawn) The peptide of claim 13 wherein the specific antigen of interest is tumor necrosis factor.
19. (Previously Presented) A pharmaceutical composition comprising as an active ingredient the polypeptide of claim 3, and a physiologically acceptable diluent or carrier.
20. (Original, Withdrawn) A pharmaceutical composition comprising as an active ingredient the peptide of claim 13, and a physiologically acceptable diluent or carrier.
- Claims 21-33. (Canceled)
34. (Previously Presented) The pharmaceutical composition of claim 19 wherein the polypeptide is predominantly monomeric.
- Claim 35. (Cancelled)
36. (Currently Amended) The pharmaceutical composition of claim ~~[[35]]~~ 34 wherein the selected phage clone is produced in E. coli as insoluble inclusion bodies and the polypeptide isolated therefrom is subsequently refolded in-vitro and purified.
37. (Currently Amended) The pharmaceutical composition of claim ~~[[35]]~~ 34 wherein the scaffold element representing the VH/VL interface comprises the sequence Lysine-44, Leucine-45, and Tryptophan-47.
38. (Currently Amended, Withdrawn) The pharmaceutical composition of claim ~~[[35]]~~ 34 wherein the CDR3 sequence between residues 95 and 100C comprises the consensus sequence: Gly-X-Ser-Pro-Gln (SEQ ID NO: 6), wherein X represents any amino acid.
39. (Currently Amended, Withdrawn) The pharmaceutical composition of claim ~~[[35]]~~ 34 wherein the CDR3 sequence between residues 95 and 100C is selected from the sequences: Gln-Ser-Gly-Gln-Ser-Pro-Gln-Ser-Ile (SEQ ID NO: 9), and Asn-Gly-Lys-Ser-Pro-Gln-Ala-Ala-Trp (SEQ ID NO: 8).

40. (Previously Presented) The pharmaceutical composition of claim 19 wherein the CDR3 sequence between residues 95 and 100C comprises the sequence: Phe-Pro-Thr-Gly-Asp-Leu-Ala-Glu-Lys (SEQ ID NO: 7).

41. (Previously Presented, Withdrawn) The pharmaceutical composition of claim 19 wherein the specific antigen of interest is Streptavidin.

42. (Previously Presented, Withdrawn) The pharmaceutical composition of claim 20 wherein the polypeptide is encoded by a polynucleotide isolated from a phage clone selected from a phage-display library comprising a plurality of recombinant phage, each of said recombinant phages having an expression vector encoding a single-domain of the variable region of the heavy chain of an antibody molecule comprising a natural framework scaffold of a mammalian monoclonal antibody without induced mutations or modifications in the original VH/VL interface framework residues, said VH/VL interface comprising a Lys residue at position 44, a Leu residue at position 45, and a Trp residue at position 47 and a randomized CDR3.

43. (Previously Presented, Withdrawn) The pharmaceutical composition of claim 20 wherein the peptide comprises 4-20 amino acids.

44. (Previously Presented, Withdrawn) The pharmaceutical composition of claim 20 wherein the peptide comprises 7-15 amino acids.

Claim 45. (Cancelled)

46. (Previously Presented) The polypeptide of claim 1 wherein the residue at position 44 is Lys.

47. (Previously Presented) A pharmaceutical composition comprising as an active ingredient the polypeptide of claim 1, and a physiologically acceptable diluent or carrier.